5-15-2000

DATA EVALUATION RECORD

STUDY 2

CHEM 275100 Buprofezin §161-2
CAS No. 69327-76-0
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44463102
Rupprecht, J. K. 1997. Photodegradation of buprofezin: a summary of photolysis under natural sunlight and artificial sunlight. Laboratory Project ID: 516BF. Unpublished study performed by Nihon Nohyaku Co., Osaka, JAPAN and Exxon Biomedical Sciences, East Millstone, NJ; and submitted by AgrEvo USA Co., Pikeville, NC.

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CONCLUSIONS

Degradation - Photodegradation in Water

1. The reported studies (one with natural sunlight and one with artificial sunlight) do provide some useful information on the aqueous photodegradation of buprofezin. The following are noted as deviations from the Subdivision N guidelines:

a. The use of mercury vapor lamp as artificial light source: EFED only recommends studies conducted with natural sunlight or with xenon-arc lamp as an artificial light source. The use of mercury vapor lamp is strongly discouraged mainly due to the discontinuity in the radiation source, especially in the 290 to 800 nm range. However, since (1) the mercury vapor lamp was of medium and high pressure (it was equipped with a Pyrex sleeve to filter any irradiation at wavelengths below 290 nm); (2) a chemical actinometer (p-NAP) was used to calibrate the intensity of this light system to that of normal sunlight; and (3) buprofezin absorbance maxima is at approximately 246 nm, with minimal absorbance at wavelengths greater than 290 nm, the use of mercury vapor lamp as an artificial light source could be considered acceptable.

b. Only individual replicates were used for each sampling interval in the calculation of half-lives of the artificial light system.

c. Temperature and pH were not controlled in the natural light system.

Nonetheless, a similar pattern of degradation for buprofezin was observed in both the natural sunlight and the artificial light, as well as the formation of same degradates. Furthermore, since photodegradation does not seems to be a rapid process for this chemical as indicated by its absorbance maxima, the submitted studies could be used to determine the rate of photolysis of buprofezin and the rate of formation/decline and the identity of buprofezin degradates.

These studies can be used to fulfill the EPA data requirements on hydrolysis. No additional data is required.

2. Uniformly phenyl ring-labeled [^{14}C]buprofezin, at a nominal concentration of 0.1 ppm, degraded with a registrant-calculated half-life of 33 days in distilled deionized water irradiated with natural sunlight and maintained at 15.8-31.3°C during June at 34°N latitude. In contrast, the parent compound was stable in the dark controls. However, the half-life in the irradiated solution is questionable because too few data points were used (three) and the half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. Additionally, a constant temperature was not maintained nor was the pH held constant. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. In the irradiated solution, the parent compound was initially 93.1% of the applied radioactivity, decreased to 77.9% by 10 days posttreatment, and was 55.0% at 30 days. In contrast, in the dark control, 92.6% of the applied radioactivity remained as parent following 30 days of incubation. In the irradiated solution, the major degradate BF-21

days posttreatment. The minor degradate BF-11 was a maximum of 2.2% of the applied radioactivity at 30 days posttreatment. Seven minor degradates (BF-2, BF-9, BF-10, BF-12, BF-16, BF-19 and BF-25) were each present in the irradiated solution at ≤1.1% of the applied radioactivity throughout the incubation period. In the dark control, the minor degradates BF-21 and BF-11 were maximums of 4.2% (30 days) and 2.5% (15 days) of the applied radioactivity, respectively. Three minor degradates (BF-2, BF-10 and BF-12) were each present in the dark control at ≤1.0% of the applied radioactivity in the dark control throughout the incubation period. Four of the minor degradates detected in the irradiated solution (BF-9, BF-16, BF-19 and BF-25) were not detected in the dark controls.

Nonradiolabeled buprofezin, at a nominal concentration of 0.27 ppm, degraded with a registrant-calculated half-life of 38 sunlight equivalent days ($r^2 = 0.86$; 40°N at mid-summer) in pH 9 aqueous buffer solution that was irradiated continuously with a mercury vapor lamp and maintained at 25 ± 5°C for up to 165.5 hours. In contrast, the parent compound was stable in the pH 9 dark controls. However, the half-life in the irradiated solution is questionable because individual replicates were used for each sampling interval and material balances were not determined. Additionally, the half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. In the irradiated solution, the parent compound was initially present at 0.24 ppm, decreased to 0.18 ppm by 48 hours posttreatment, and was 0.13 ppm at 165.5 hours. In contrast, in the dark control solution, the parent was 0.23 ppm (97% of the initial concentration) following 165.5 hours of incubation. Tabular data on the pattern of formation and decline of the degradates were not reported. In the irradiated solution, the major degradate BF-21 was present at 0.0095 ppm at 165.5 hours posttreatment. The minor degradate tentatively identified as BF-12 was present at 0.0042 ppm at 165.5 hours posttreatment, and three minor degradates (tentatively identified as BF-9, BF-10 and BF-11) were each estimated to be present at ≤0.0029 ppm throughout the incubation period.

METHODOLOGY

The photolysis of buprofezin {2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1,3,5-thiadiazin-4-one} was studied in deionized water under natural light irradiation using uniformly phenyl ring-labeled [^{14}C]buprofezin, and in pH 9 (0.013 M borate) aqueous buffer solution under artificial light irradiation using nonradiolabeled buprofezin.

Natural Light System

Uniformly phenyl ring-labeled [^{14}C]buprofezin (radiochemical purity >98%; specific activity 22.5 μCi/mg; p. 24), dissolved in distilled, deionized water at a nominal concentration of 0.1 ppm, was filter-sterilized (0.45 μm) and added to quartz glass tubes

(p. 25). The tubes were stoppered and irradiated with natural sunlight in June (Osaka, JAPAN; latitude 34° 27' N) for up to 30 days. The average duration of direct sunlight exposure throughout the incubation period was 5.5 hours per day (p. 15). The intensity of the sunlight was not reported (see Comment #6). The temperature of the test solutions was not controlled; ambient temperatures varied 4-12°C each day between 15.8°C and 31.8°C (Appendix III, p. 76). Control samples were wrapped in aluminum foil and incubated in darkness for up to 30 days. Duplicate irradiated and dark control samples were removed for analysis at 0, 10, and 30 days posttreatment.

At each sampling interval, an aliquot of each sample was analyzed for total radioactivity by LSC (p. 16). The remaining sample solution was partitioned twice with ethyl acetate. Aliquots of the combined aqueous and organic fractions were analyzed by LSC. The remainder of the ethyl acetate fraction was treated with anhydrous sodium sulphate and concentrated until dry. Residues were re-dissolved in methanol and analyzed by two-dimensional TLC on silica gel plates developed using the solvent systems: (1) diisopropyl ether:acetone (9:1, v:v) and (2) benzene:ethyl acetate:acetic acid (6:2:1, v:v:v; p. 26). Extracts were co-chromatographed with nonradiolabeled reference standards which were visualized under UV light (wavelength not reported). The areas of radioactivity were determined by autoradiography, then were scraped from the plates and analyzed by LSC.

Artificial Light System

Nonradiolabeled buprofezin, dissolved in dimethyl formamide, was added at a nominal concentration of 0.27 ppm to sterilized pH 9 (0.013 M borate) aqueous buffer solution (p. 14). Aliquots of the treated buffer solution were placed in autoclaved quartz test tubes which were stoppered without headspace; approximately half the tubes were wrapped in foil to serve as dark controls. The tubes were maintained at 25 ± 5°C and irradiated continuously for up to 30 days by a mercury vapor lamp with a Pyrex sleeve to filter out wavelengths below 290 nm (p. 43). Total light exposure for the study was determined to be equivalent to 32.1 days of summer sunlight at 40°N by chemical actinometer solution (Appendix F; pp. 63, 64); the average light intensity and total light intensity were not reported (see Comment #6). Individual samples of the irradiated solution were removed for analysis at 0, 5.5, 21.5, 48, 70, 75.8, and 165.5 hours posttreatment (p. 16); dark controls were removed for analysis at the same intervals with the exception of 5.5 hours. The pH was measured at each sampling interval.

Samples were extracted by shaking with toluene. The toluene fraction was separated and analyzed for the parent by GC with flame ionization detection (p. 57); the system was calibrated with reference standards. To confirm degradate identities, aliquots of samples were acidified (pH 5.6) and passed through a preconditioned ENVI™-Carb solid phase extraction (SPE) column. The compounds of interest were eluted from the columns using methanol and methylene chloride (p. 59). The combined eluents were concentrated and reconstituted with methanol. Triplicate aliquots were analyzed by HPLC (Waters C18

column) using a mobile phase of water:acetonitrile (60:40; v:v) with UV detection (246 nm). Additional degradate confirmation was performed using GC with mass selective detection in the electron impact mode (p. 62).

A p-NAP/pyridine actinometer solution was prepared to compare the intensity of the artificial light source with that of normal sunlight. The actinometer solutions were analyzed by HPLC (Bondapak or Waters Nova-Pak C18 column) using a mobile phase of acetonitrile:1% acetic acid (50:50, v:v) with UV detection (280 nm; Appendix B, p. 58). The equivalency of the artificial light source was determined to be 0.19 days of natural sunlight (at 40°N and at mid-summer) per hour of artificial light irradiation; the registrant-calculated half-life was converted to sunlight equivalent days.

DATA SUMMARY

Natural Light Study

Uniformly phenyl ring-labeled [^{14}C]buprofezin, at a nominal concentration of 0.1 ppm, degraded with a registrant-calculated half-life of 33 days in distilled deionized water irradiated with natural sunlight from 15.8-31.3°C during June at 34°N latitude (p. 18). In contrast, the parent compound was stable in the dark controls. However, the half-life in the irradiated solution is questionable because too few data points were used (three) and the half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data (see Comment #1). Additionally, a constant temperature was not maintained and the pH was not held constant (see Comments #5, 2). All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. In the irradiated solution, the parent compound was initially present at 93.1% of the applied radioactivity, decreased to 77.9% by 10 days posttreatment, and was 55.0% at 30 days (Appendix I; Table 2, p. 30). In contrast, in the dark control, 92.6% of the applied radioactivity remained as parent following 30 days of incubation. In the irradiated solution, the major degradate

N-phenylformamide (BF-21)

was initially present at 3.5% of the applied radioactivity, increased to 5.9% by 10 days posttreatment, and was a maximum of 9.7% at 30 days. The minor degradate (N-1,1-dimethylethyl)-2-(1-methylethyl)-N'-phenylimidodicarbonic diamide (BF-11) was a maximum of 2.2% of the applied radioactivity at 30 days posttreatment. Seven minor degradates 2-[(1,1-dimethylethyl)imino]tetrahydro-5-(4-hydroxyphenyl)-3-(1-methylethyl)-4H-1,3,5-thiadiazin-4-one (BF-2); dihydro-3-(1-methylethyl)-5-phenyl-2H-1,3,5-thiadiazine-2,4(3H)-dione (BF-9); 2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1,3,5-thiadiazin-4-one 1-oxide (BF-10); N-(1-methylethyl)-N'-phenylurea (BF-12); phenylurea (BF-16); 6-[(1,1-dimethylethyl)amino]-2,3-dihydro-3-

phenyl-4H-1,3,5-thiadiazin-4-one (BF-19); and N-[[(1,1-dimethylethyl)amino] thioxomethyl]-N-(1-methylethyl)-N'-phenylurea (BF-25) were each present at ≤1.1% of the applied radioactivity throughout the incubation period. Unidentified radioactivity consisting of residual radioactivity plus unidentified minor degradates was a maximum of 15.5% of the applied radioactivity at 30 days posttreatment. In the dark controls, the minor degradates BF-21 and BF-11 were maximums of 4.2% (30 days) and 2.5% (15 days) of the applied radioactivity, respectively. Three minor degradates (BF-2, BF-10 and BF-12) were each present in the dark control at ≤1.0% of the applied radioactivity throughout the incubation period. Unidentified radioactivity in the dark control was a maximum of 5.5% of the applied radioactivity at 30 days posttreatment. Four of the minor degradates detected in the irradiated solution (BF-9, BF-16, BF-19 and BF-25) were not detected in the dark controls.

Material balances were 94.9-103.9% for the irradiated solutions and 100.1-107.1% for the dark controls throughout the incubation period (Table 2, p. 30).

Artificial Light Study

Nonradiolabeled buprofezin, at a nominal concentration of 0.27 ppm, degraded with a registrant-calculated half-life of 38 sunlight equivalent days (40°N at mid-summer; r^2 = 0.86; p. 65; Figure 2, p. 51) in pH 9 aqueous buffer solution that was irradiated continuously with a mercury vapor lamp and maintained at 25 ± 5°C for up to 165.5 hours. In contrast, the parent compound was stable in the pH 9 dark control solutions. However, the half-life in the irradiated solution is questionable because individual replicates were used for each sampling interval and material balances were not determined (see Comment #1). Additionally, the half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. In the irradiated solution, the parent compound was initially present at 0.24 ppm, decreased to 0.18 ppm by 48 hours posttreatment, and was 0.13 ppm at 165.5 hours (Table 1, p. 49). In contrast, in the dark control solution, the parent was present at 0.23 ppm (97% of the initial concentration) following 165.5 hours of incubation. Tabular data on the pattern of formation and decline of the degradates was not reported (see Comment #6). In the irradiated solution, the minor degradate N-phenylformamide (BF-21) was present at 0.0095 ppm at 165.5 hours posttreatment (p. 47; see Comment #9). The minor degradate tentatively identified as N-(1-methylethyl)-N'-phenylurea (BF 12) was present at 0.0042 ppm at 165.5 hours posttreatment (p. 46). The three minor degradates tentatively identified as (dihydro-3-(1-methylethyl)-5-phenyl-2H-1,3,5-thiadiazine-2,4(3H)-dione (BF-9); 2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1,3,5-thiadiazin-4-one 1-oxide (BF-10); and (N-1,1-dimethylethyl)-2-(1-methylethyl)-N'-phenylimidodicarbonic diamide (BF-11) were each estimated to be present at ≤0.0029 ppm throughout the incubation period.

Material balances were not determined.

COMMENTS

1. The registrant-calculated half-lives of the parent in the natural and artificial light systems were questionable due to inadequacies in the experimental method as well as in the data used to calculate the half-lives. In the natural light system, too few sampling intervals (three) were used in the calculation of the half-life, and environmental variables (temperature and pH) were not controlled during the study. In the artificial light system, the temperature was not controlled during the study, material balances were not determined, and only a single test vessel was removed for analysis at each sampling interval. The use of a single treated solution is generally not considered to be good laboratory practice. At a minimum, duplicate samples are necessary for the valid determination of a half-life. Additionally, the half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data for each system.

2. Test solutions in the natural light system were not buffered as required by Subdivision N Guidelines, and the pH was not measured, precluding a determination of a constant pH being maintained throughout the study. In the natural light system, distilled deionized water was utilized which is expected to have an approximate pH of 7. The study author stated that a photolysis study conducted at a pH of 7-9 represents a hydrolytically stable pH range for buprofezin (p. 17). The reviewer notes that, in order to accurately compare the artificial and natural light systems, as attempted in the study, both systems should have been buffered at the same hydrolytically stable pH and incubated under similar conditions with the exception of the light source.

3. Material balances were not provided for the artificial light study. Material balances are necessary to demonstrate that the loss of parent material was the result of degradation and not other physical phenomena such as volatilization or sorption to the test apparatus. Additionally, material balances are necessary to allow the reviewer to confirm that all major degradates (residues present at $\geq 10\%$ of the applied test material) were identified, as required by Subdivision N Guidelines.

4. Complete data on the formation and decline of degradates were not reported for the artificial light system (which utilized nonradiolabeled parent), as required by Subdivision N Guidelines. The reviewer had to acquire data from the text to report the final concentrations (the only ones reported in the study) of the degradates present at the end of the incubation period. In future studies, complete residue characterization data should be provided (in tabular form) to allow clear and concise review of the study. The study author stated that the concentrations of several tentatively identified minor degradates were estimated because they were present at concentrations too low to be confirmed by GC/MS or to be integrated by HPLC (p. 46). Four of the degradates detected in the natural light system (BF-2, BF-16, BF-19 and BF-25) were not specified as being detected in the artificial light system.

5. A constant temperature was not maintained in each of the test systems. In the natural light study, the apparatus was maintained outdoors and the temperature ranged from 15.8 to 31.3°C. In the artificial light study, temperature was maintained at 25 ± 5°C. Subdivision N Guidelines require that the temperature be maintained at 25 ± 1°C.

6. The light sources were not adequately characterized. In the natural sunlight system, the sunlight intensity and wavelength distribution were not provided. In the artificial light system, the intensity and wavelength distribution of the mercury vapor lamp were not compared with those of natural sunlight. The reviewer notes that a chemical actinometer solution was utilized to equate the intensity of the artificial light source with that of natural sunlight. The equivalency of the artificial light source was determined to be 0.19 days of natural sunlight (at 40°N and at mid-summer) per hour of artificial light irradiation.

7. Method detection limits were not reported. It is necessary that both limits of detection and quantitation be reported to allow the reviewer to evaluate the adequacy of the method for the determination of the test compound and its degradates.

8. The water solubility of the test compound was reported as 0.463 mg/L at pH 9 at an unspecified temperature (p. 41).

9. Based on a comparison between the chemical structures in Figures 1 and 7 (pp. 7, 56), the reviewer determined that the degradates BF-9, BF-10, BF-11, BF-12 and BF-21 reported in the natural light study were equivalent to the degradates A11, A12, A14, A3 and formanalide reported in the artificial light study; therefore, the names from the natural light system were used for both systems in this DER.

10. The reviewer notes that in both the natural and artificial light systems, buprofezin is susceptible to direct photolysis in water; however, due to the deficiencies stated previously, additional studies are necessary to accurately determine the degradation rate of buprofezin and the patterns of formation and decline of the degradates in a buffered aqueous solution.

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